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CAUSATION OF THE HEART-BEAT

AND

OTHER PROBLEMS IN CARDIAC PHYSIOLOGY.

BY

T. WESLEY MILLS, M.A., M.D., L.R.C.P., Eng.,
Professor of Physiology, McGill University.

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THE CAUSATION OF THE HEART-BEAT AND OTHER PROBLEMS IN CARDIAC PHYSIOLOGY.

By T. Wesley Mills, M.A., M.D., L.R.C.P., Eng.,
Professor of Physiology, McGill University, Montreal.

Until very recently, nearly all investigations on the physiology of the heart were made on mammals. This was the case even in scientific Germany, and is explicable by the fact pointed out by Professor Carl Semper, that physiologists being mostly connected with the medical faculties of the universities were led to regard the chief, if not the sole purpose of physiological study to be the advancement of clinical medicine ; consequently their investigations were confined to the mammalian heart, as the one most likely to throw light on the cardiac physiology of man. To this statement the heart of the frog is an exception. It has long been studied by physiologists in all countries ; but even so late as six years ago very little was known of the hearts of other animals from the physiologist's point of view.

It has generally been found that science best ministers to man's material wants in the end if left free to develop itself, as science, totally independent of immediate practical application. It will in such case fall into the hands of the most competent and reliable investigators.

To commence the solution of cardiac problems with the most complex of all hearts—the mammalian—was a most unphilosophical proceeding, especially in this day of evolutionary light. If mammals have been derived from lower forms of life, it follows, at least as the very strongest probability, that their hearts are ancestrally represented in the hearts of lower forms; if so, then plainly the study of the mammalian heart should begin with that of antecedent and simpler developments.

I hope to be able to show that the researches of the last few years have not only thrown a flood of light on cardiac physiology and anatomy in general, but brought us incomparably nearer to a correct appreciation of the complex workings of the mammalian heart itself than we were even three years ago.

The work for the mammalian heart along the new lines of departure in investigation is still in great part to be done. The problem I wish especially to attack in this paper is the cause, or rather causes, of the heart-beat. These have now been fairly well determined for the lower vertebrates. In the light thus afforded, what may we consider as the probable solution of the question for the mammalian heart? The study of this problem will involve, incidentally, that of many others.

When one considers the evolution of the heart morphologically, we are brought back to its beginnings, in connection at least with a nutritive fluid, in contractile tubes, as in the worms among invertebrates; and it would appear that most, if not all, kinds of hearts may be considered as dilations and differentiations of this simple form of pulsatile organ.

Passing by the pulsating vacuoles of the Infusorians as of doubtful significance, the contractile tube seems to be the primitive representative of the heart; and it is very significant that the earliest form of the heart in the embryo of the highest vertebrates is a pulsating tube, the after-changes in which give an epitomized history, to a large extent we may suppose, of the evolution of the vertebrate heart from lower forms.

Moreover, in that lowest of fishes (?), the Amphioxus, the heart is represented by pulsatile vessels. Now in these pulsatile tubes, so far as I know, nervous elements have not been found. The heart of the chick beats on the second day of incubation, when no nervous structures are to be found in it any more than in an Amœba.

Englemann has shown that in the ureter (or a portion of it), and Luchsinger in the veins of the bat's wing, there is automatic contraction of muscular tissue in the entire absence of nervous elements.

Ransom has been unable to find in the heart of the snail (*Helix*) any ganglion cells. This investigator's work on the heart of the Poulp (*Octopus*) has, it seems to me, thrown great light on the whole subject of cardiac physiology. A brief notice of it in this place may be instructive.

The heart in this creature belonging to the most highly developed class of mollusks, the Cephalopods, consists of: (1) a pre-branchial or venous portion, and (2) a post-branchial or arterial portion. The former includes the vena cava, kidney veins, and branchial heart; the latter the auricles and ventricle.

The pre-branchial system collects blood from the veins and drives it through the gills. Two large nerves known as the visceral, and representing the vagi, are given off to the heart. On the auricles, the branchial heart and the gills there is a ganglion connected with the main nerves. The muscular tissue of the ventricle is finely striated; of the auricles, smooth. After the most careful microscopic examination, Ransom asserts the entire *absence* of nerve cells in the substance of the heart of this mollusk. He considers that the ganglia lying on the heart have nothing to do with originating nervous impulses that might serve to cause cardiac pulsation. He believes that they have a co-ordinating influence over the various parts of the cardiac system, and probably act reflexly; after their excision, the heart still beats, but not in normal fashion.

The contractile kidney veins are composed of smooth muscle cells, devoid of ganglia anywhere in their substance.

Long since Bernstein, and more especially Bowditch, showed that the lower two-thirds of the frog's ventricle do not possess the power to contract *automatically*. It has, however, been shown that if this portion of the ventricle be tied upon a perfusion cannula, and some fluid, if only weak saline solution, be passed through it, this quiescent apex will commence to beat when the pressure within it has reached a certain point.

Ransom points out that in the Poulp the heart, and especially the regulative part of the cardiac muscular machinery, the ventricle in this instance, is remarkably sensitive to changes in intra-cardiac pressure.

In my own papers on the Fish and Menobranchus, attention has been called to the readiness with which the heart, especially of fishes, is influenced by even slight changes in intra-cardiac pressure.

Some years ago Roy showed that the work of the heart of the frog is largely dependent on the action of the auricles.

This, taken in connection with other facts more recent, seems to point to intra-cardiac pressure as *one* determining cause of the beat, especially of the ventricle, even in the mammalian heart.

Gaskell has shown that in the Chelonian heart there are circular rings of fibres between its different divisions, and points to these as evidence of structural continuity, explaining the physiological continuity of the beat of the different parts of the tortoise heart.

That the Chelonian heart beats for a time fairly well in the absence of all fluid shows that the intra-cardiac pressure is not an absolutely *essential* factor in this form of heart.

But I have pointed out that a hæmorrhage which would affect but little the beat of the Chelonian heart *arrests* that of the fish. It will thus appear that a factor which may be of the greatest importance in explaining the beat in one form of heart may be of little consequence in others.

Again, Ransom has shown that the different parts of the heart of the Poulp are not structurally continuous as regards muscular tissue, but that between the main divisions of the heart there are zones of connective tissue. But one of the most remarkable examples of both physiological and structural continuity is to be seen in the shark and ray tribe of fishes. As I have pointed out in my paper on the heart of the fish (*Journal of Physiology*, Vol. VII), there seems to be no limit to the ease with which a reversed rhythm may be set up by a slight stimulus to the contractile bulbus.

The heart of the fish seems to be by far the most *sensitive* heart among vertebrated animals, as I have shown in various ways. This heart is often completely and, indeed, permanently arrested by a highly *venous condition* of the blood ; and again and again have I been surprised at noticing the ease with which the whole cardiac machinery can be restored to good behaviour when thus arrested, on giving the fish a fresh supply of oxygen by placing the gills in water.

This, then, brings us to another factor in the causation of the cardiac beat—viz., the character of the nutritive fluid ; and here once more we find the greatest difference in various forms of heart as to the influence of this factor—indeed, differences in individual animals of the same species. What would but little affect a Chelonian heart would suffice to arrest that of the fish ; and the same I have shown to hold for Menobranchus (our Canadian water newt.)

The old notions of the influence of the nervous factor in the causation of the cardiac beat having been greatly disturbed, it remains to inquire what views we are justified in adopting in the light of recent advances. We have seen that intra-cardiac nerve cells are not essential to the heart-beat *per se*, for in some hearts no such cells are found.

Leaving these ganglionic cells for the present, we may inquire what relation the *nerves* distributed to the heart bear to its normal beat. The recent extensive researches on the influence of the vagus nerve on the heart, in the frog by Heidenhain and by Gaskell ; on the land tortoise by the latter ; and on the Terrapin and Sea-turtle by myself, have put the vagus in an entirely new light. To these results some previous reference has been made in this JOURNAL (Jan. 1886).

It has been shown that whatever may be the constant action of the vagus, it can, under stimulation, greatly modify the heart's action—always in the way of final augmentation or improvement of rhythm ; and I have myself shown that the degree of its beneficial action is *directly proportional to the heart's needs*. This seems to apply to almost all, if not all, the animals as yet examined that have a vagus or closely analagous nerve. It holds, *e.g.*, for the visceral nerve of the Poulp.

Various theories have been from time to time proposed to account for the action of the vagus.

Heidenhain spoke of depressor and augmentor fibres. Gaskell rejected this explanation and held to a "trophic" action of the vagus, entering into a very elaborate explanation of the relation of the inhibitory phase and the after augmentation phase of the heart's action. Later, he has shown that in the frog there are two sets of fibres with different action, and that these fibres are respectively inhibiting fibres proper, which are medullated, and sympathetic fibres which are non-medullated.

Gaskell thought that in the *Crocodilia* he had found a vagus that was a pure depressor; but this I have shown in my paper on the Alligator (*Jour. of Anat. and Phys.*, Vol. XX) to be an error. The vagus in the crocodile tribe is similar in action to that in the Chelonians, etc.

I believe I was myself, however, the first to call attention, in a published paper, to general physiological resemblances between the main sympathetic chain in which the cardiac accelerators run, and the vagus. I pointed out (paper on Terrapin) that stimulation of this chain led to results similar to those obtained by stimulation of the vagus itself, and, indeed, that the same law applied—the worse the cardiac rhythm the more marked the influence. I also called attention to some after-effects (in some cases primary effects)—viz, irregularity or brief stops of the heart which were then difficult to explain. We know now that the two kinds of fibres, inhibitory proper and sympathetic, have in some respects an opposite action on the heart.

Throughout I have maintained that we must look finally for an explanation of these effects in chemistry, in tissue metabolism. Ransom proposed a problem which has since been, in part at least, solved—*i.e.*, solved up to the crucial point. He says:

"If it could be shown that the true vagus fibres of a tortoise or frog in any way tend to increase constructive metabolism, while the sympathetic favored the destructive processes, a step would already be taken in harmonizing the phenomena presented by mollusca and vertebrata and in forming a general interpretation applicable to all."

Gaskell now thinks he has facts which lend strong support to such a view, though I find no mention in his latest paper of this conception as Ransom's; nor, indeed, any notice taken of the work of others, that has served to correct certain of his own previously published views which have later been exchanged for different ones; or that such later views had been previously announced by other investigators.

The most recent explanation in regard to the action of the vagus may then be put thus: The vagus nerve in many animals, possibly in all vertebrates, is in reality the vago-sympathetic. It contains sympathetic fibres which are motor, or whose action is associated with increased muscular contraction, followed by exhaustion; while the inhibitory fibres bring about an arrest of activity, followed by repair of function. We may express the same idea from another point of view by saying that the sympathetic fibres are functionally linked with katabolic or destructive metabolic processes, while the inhibitory fibres modify anabolic or constructive processes. Such a theory is broad, readily grasped, and from many points of view fascinating; but it is open to some objections.

I have shown that the heart of both the Terrapin and the Sea-turtle may be kept inhibited for hours by continued stimulation of the vagi nerves; in one case recorded, inhibition lasted for *six hours.* Now it is difficult to believe that so unstable a thing, as all our knowledge of protoplasm leads us to consider it, could remain in one phase of the metabolic process for six hours. I feel quite satisfied myself that the explanation of nervous and all other vital action must come largely through chemistry; but it would, perhaps, be premature to assume that the chemistry can be reduced to the simplicity indicated by the above theory. One thing is perfectly clear, the vagus and the general welfare of the heart cannot be disassociated, at least in the more complex forms of this organ.

Eichorst and Zander noted degenerative muscular changes following section of both vagi. Similar changes follow section of the nerve of a skeletal muscle. It is certain, therefore, that whether the nerves of the heart are immediately concerned in the causation of the beat or not, they are inseparably connected with the general nutritive processes of the organ. That nerves are not directly concerned in the cardiac pulsation is evident from the fact that the heart beats perfectly well when all its nerves are severed. When we have learned exactly how the nutrition of a skeletal muscle is dependent on nervous connection, we shall probably also have the explanation for the heart muscle ; possibly, also, new light thrown on many forms of cardiac disease.

The functions of the cardiac ganglia at present may be considered undetermined. Are they concerned in origination of motor impulses ? Are they co-ordinative of muscular action ? Are they regulators of nutrition ? There seems to be almost no evidence as yet for any of these views ; but there is abundant evidence that the cardiac nerves can act on the heart-muscle *directly*.

We must certainly believe that the nerves of the heart, amid the ever-varying conditions which this great central pump must meet, are in almost constant action. We must also believe that this action in health is beneficial, both because were it not so, such could never have originated in the evolution of the more complex forms of heart ; and because we find that when such influence is not exerted (as after section) the heart tissue degenerates. I have called attention to the fact that stimulation of the vagus at intervals, in a tortoise heart in which only a few fibres were seen pulsating, has led to a beat of the whole organ in a short time. Now if these few fibres could have been made to pulsate without nervous influence, would the same general result have followed ? I believe it would. The very proximity of quiescent muscle fibres, with strong tendency to beat, to others still pulsating suffices to originate in the former processes which are temporally suspended.

Gaskell has shown that if a strip of muscle from the ventricle of the tortoise be placed in a moist chamber, and a weak, interrupted current be sent through it, it will in time begin to beat and continue to do so after the stimulus is removed.

I take it that the infecting power which protoplasm of one kind has over the same or even different kinds seen in disease has its correlative in health, and that this plays a great part in the causation of the heart-beat.

Nerve is but specially modified protoplasm, and the axis cylinder is, at all events, of such a nature that its state in activity, however we conceive of that, has power to initiate or modify another condition of protoplasm in a muscle. It has been shown that in the sartorius of the frog there are two areas, one at each end, to which no nerve fibres are distributed, yet these ends contract with the rest of the muscle. Such a result is in harmony with the view I offer as to the power one protoplasmic unit has to originate in other protoplasmic units a similar condition.

Again, Roy has shown that the changes in calibre of the capillaries cannot be explained by changes of blood-pressure alone. No nervous elements have ever been found in them. Why, then, do they contract? By virtue of influences either from the lymph direct, acting chemically, or owing to altering conditions in the surrounding tissues. Here, again, one kind of protoplasm influences another by contiguity, if we may so speak. Each capillary cell is a representative in some sense of the Amœba changing under its varying environment.

The question of *spontaneous rhythm* seems to me to throw much light on the principal problem of this paper. I have carefully studied this subject in the Terrapin, the Sea-turtle (three species), the Fish and Menobranchus. In one fish of great vitality I found a remarkable power of spontaneous rhythm in every part of the heart when isolated by ligature. As regards the Chelonians, there are marked variations in different species and even individuals, but in none was there in the ventricle a very marked capacity for pulsation independent of intra-cardiac pressure, feeding or other stimulus. I am satisfied that Gaskell's statements give a highly exaggerated notion of this whole matter. But what was very striking throughout was the fact that an extremely weak stimulus sufficed to cause pulsation in parts of the heart thus isolated; and this throws much light upon the causation of the heart-beat.

Reviewing the case, which can be but inadequately discussed in one paper, it will appear that there must be various factors entering into the causation of the heart-beat in the case of the more complex hearts of higher vertebrates.

As before intimated, the cardiac physiology for mammals is yet to be worked out along the new lines; but for reasons before given, it is likely we shall find the same factors entering into the causation of the beat. In the case of each genus of animals, one or other of the factors may be more or less prominent, as has been shown.

In the light of our present knowledge, perhaps some such statement of the case as follows may be provisionally accepted :

(1.) The factors entering into the causation of the heart-beat of all vertebrates as yet examined are : (*a*) a tendency to spontaneous contraction of the muscle cells composing the heart ; (*b*) intra-cardiac pressure ; (*c*) condition of nutrition as determined directly by the blood and indirectly by the nervous supply of the organ.

(2.) The tendency to spontaneous contraction of muscle cells is most marked in the oldest parts of the heart ancestrally considered. I have shown (*Jour. of Anat. and Phys.*, Vol. XXI) that in the Sea-turtle the last segments of the ventricle to pulsate are on its extreme right ; while the right auricle outlasts the left and the sinus and great veins beat much longer still. The same has been noticed in several other groups of animals. The most recently acquired parts of the heart always are the first to lose functional activity. These are but extensions of Harvey's observations, seen in the light of evolution.

(3) In all hearts examined, intra-cardiac pressure is a factor of considerable importance ; in some, as that of the Fish, Menobranchus, etc., it is apparently the controlling factor. The same may be said of the molluscan heart.

(4) The power one contracting cell when in action seems to possess of initiating a similar state in others is of great significance.

(5) The influence of the nerves of the heart appear more and more as we ascend the animal scale. They seem only indirectly concerned in the causation of the beat by their influence over nutritive processes ; but as the heart is being so frequently modified in its action, their influence in highly developed hearts becomes an almost constant factor, and of a degree of importance which our knowledge of the relation of nerve to muscle enables us but inadequately to appreciate, but which the pathological changes ensuing on nerve section illustrate.

(6) It almost follows from the above that one part of the

heart having contracted the other parts must follow. This is probably the explanation of the rapid onset of the ventricular after the auricular systole in the mammal. It will be remembered, too, that even in the mammal contraction begins in the great veins entering the heart.

The basis of all these explanations is found, in reality, in the *natural contractility of protoplasm.* A heart in its most developed condition still retains, so to speak, the inherited but modified Amœba in its every cell.

It seems likely to be shown that in the causation of the beat of the mammalian heart all the above-mentioned factors enter.

In conclusion, I would express my conviction that our present explanations of heart disease are of too mechanical a character; the nervous and the other factors indicated should more largely enter into the reckoning in the cardiac pathology of the immediate future.